which were isolated from the patients presented with enteric fever during 1990 to 2015. Antimicrobial susceptibility testing was done by disk diffusion method as per CLSI 2015 and MICs were determined by E test method as per manufacturer's guidelines (AB Biodisk, Sweden).

For molecular chaeacterization of azithromycin resistance, PCR detection was done to screen for the presence of genes responsible for azithromycin resistance i.e, *ereA, ereB, ermB, mefA, mphA, mphB and mphD* from plasmid and genomic DNA. Sequence analysis was done to detect mutations in *acrR, rlpD and rlpV* from genomic DNA.

Results: It was observed that 96.11% of the isolates were susceptible to azithromycin using disk diffusion method. There was a linear trend observed with time in azithromycin susceptibility (χ^2 = 5.240, P value <0.02). The MIC 50 and MIC 90 values were 6 and 12 μg/ml respectively while the resistance breakpoint is ≥16 μg/ml. There was no acquired gene for macrolide resistance in plasmid or genomic DNA of any isolate and DNA sequences of *acrR, rlpD and rlpV* genes did not show any mutations.

Total use of azithromycin in pediatric population was only 13,125 mg given to 16 patients in 2014-15.

Conclusion: Azithromycin is a good promising agent against typhoid fever on the basis of MIC distribution in India at present. More studies are required to study the use of azithromycin in complicated infections as at present it is being used only for uncomplicated cases.

http://dx.doi.org/10.1016/j.ijid.2016.02.316

Type: Poster Presentation

Final Abstract Number: 41.123
Session: Poster Session I
Date: Thursday, March 3, 2016
Time: 12:45-14:15
Room: Hall 3 (Posters & Exhibition)

In vitro and in vivo activity of "compound A" against gram-positive and -negative pathogens including MDR strains

T.K. Burman [1], P. Bhateja [1], S. Dube [1], A. Soni [2,*]

[1] *Daiichi Sankyo India Pharma Private Limited, Gurgaon, Haryana, India*
[2] *India*

Background: Compound A is a novel Topo-IV inhibitor with broad spectrum activity against both Gram- negative and positive pathogens, especially *Pseudomonas aeruginosa*, *Acinetobacter. baumannii, Escherichia coli*, and MRSA. The present study focuses on its *in vitro* activity, *in vivo* efficacy and pharmacokinetics-pharmacodynamics in murine infection models.

Methods & Materials: MIC were determined by CLSI method against 135 bacterial strains including ATCC and clinical isolates of (sensitive and MDR) *Pseudomonas aeruginosa* (n=55), *A. baumannii* (n=25), *Escherichia coli* (n=30) and MRSA (n=25) including MDR isolates. Time kill study was performed against these pathogens. The therapeutic efficacy was evaluated using a mouse pulmonary infection model. The pharmacokinetics-pharmacodynamics (PK-PD) parameters against *P. aeruginosa* were determined in neutropenic murine thigh infection model.

Results: Compound A showed MIC_{90} of 4, 0.5, 0.25 and 0.25 μg/ml against *P. aeruginosa*, *A. baumannii*, *E. coli* and MRSA, respectively. In murine pulmonary infection model, it showed killing potential against *P. aeruginosa* and *A. baumannii* and reduced the pulmonary bacterial number in a dose-dependent manner. In the PK-PD study, the efficacy of Compound A against *P. aeruginosa* infection was correlated with AUC/MIC (R^2 = 0.89) and Time above MIC (R^2 = 0.93) more than Cmax/MIC (R^2 = 0.12).

Conclusion: Compound A exhibited excellent broad spectrum of activity against Gram- positive and negative pathogens. Hence, it could be a promising investigational candidate for antibacterial therapy.

http://dx.doi.org/10.1016/j.ijid.2016.02.317

Type: Poster Presentation

Final Abstract Number: 41.124
Session: Poster Session I
Date: Thursday, March 3, 2016
Time: 12:45-14:15
Room: Hall 3 (Posters & Exhibition)

A small molecule that inhibits FtsZ with potent in vitro and in vivo activity against staphylococcus aureus

S. Dube [1,*], T. Mathur [1], M. Kumar [2]

[1] *Daiichi Sankyo India Pharma Private Limited, Gurgaon, Haryana, India*
[2] *Daiichi Sankyo India Pharma Private Limited, Gurgaon, India*

Background: The emergence of bacterial resistance to antibiotics is a major concern; therefore, it is critical to develop new antibiotics with novel modes of action. FtsZ is an essential bacterial guanosine triphosphatase (GTPase) play an essential role in bacterial cell division, and its homologs are present in almost all eubacteria, archaea and mammalian that polymerizes and assembles into a ring to initiate cell division. Compound-A is a novel FtsZ inhibitor with potent and selective *in vitro* bactericidal activity against methicillin-susceptible *Staphylococcus aureus* (MSSA) methicillin-resistant *Staphylococcus aureus* (MRSA).

Methods & Materials: The antibacterial activities were determined by the CLSI micro-broth dilution methods. *In vivo* efficacy was evaluated in mouse model of infection caused by MRSA.

Results: Compound-A showed potent activity against various clinical isolates of MSSA and MRSA. The MIC_{90s} of Compound-A against MRSA was 2 μg/mL, respectively. Compound-A showed the potent inhibitory activity against *S. aureus* FtsZ enzyme >100 fold selection against its mammalian homolog porcin β-tubulin. Compound- A showed bactericidal activity against MRSA and showed synergy with carbapenem drugs. Compound-A was efficacious in mouse infection model.

Conclusion: Compound-A showed potent activity against multidrug resistant MRSA strains and bactericidal activity. These results suggest that Compound-A is suitable for further investigation.

http://dx.doi.org/10.1016/j.ijid.2016.02.318